

Rapid Assay of Protein Folding

Geoffrey S. Waldo

Our rapid assay of protein folding uses the folding of a green fluorescent protein (GFP) to monitor the folding of a test protein. It does this by linking the two proteins in a hybrid molecule with the characteristics of both. When the hybrid is synthesized in a host cell or cell-free extract, the GFP achieves its fluorescent capability only if proper folding has taken place. Because robust folding is an excellent indicator of solubility, our method enables researchers to identify—quickly and easily—the soluble proteins necessary for research into protein structure and function.

Applications

The primary application for this technology is as a high-throughput analytical tool for identifying the soluble proteins needed for

- medical research,
- drug discovery and improvement,
- chemical industrial processes, and
- basic research into the structure and function of proteins.

The technology is equally applicable to directed evolution techniques for improving protein solubility, opening the door for these techniques to be used on all proteins.

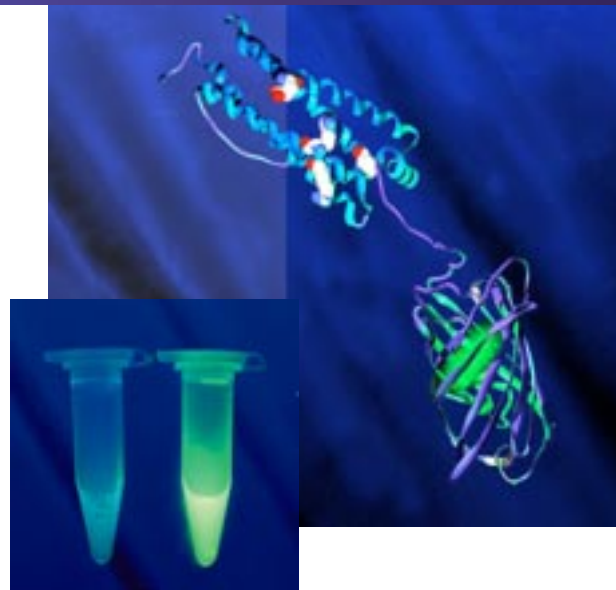
Benefits

The rapid assay of protein folding provides the following benefits:

- support for high-throughput analyses for examining large numbers of proteins;
- a fluorescent indicator proportional to the amount of soluble protein in a sample;
- the capability to determine protein folding and solubility in single cells, cell colonies, and cell-free extracts.

Because this method works for all proteins, even when function is unknown, it

- exploits techniques, materials, and equipment already familiar to molecular biologists; and
- eliminates the need for external reagents, which are costly and sometimes toxic.



The folding assay enables rapid identification of soluble proteins and their genetic variants for high-level production of research proteins and for directed evolution to improve protein folding. Our method links a test protein (X, top left) to the green fluorescent protein (GFP, lower right). If X folds properly during synthesis, the GFP also folds properly and achieves its native shape and function. It will then fluoresce under an ultraviolet or blue light. In this way, GFP's fluorescent capabilities serve as an indicator of X's folding and, therefore, its solubility. This simple assay eliminates many time-consuming steps and works for essentially all proteins in different formats, including cell-free extracts (test tubes, bottom left inset).

All applications are available for commercial licensing.

Technical contact:
Geoff Waldo, waldo@lanl.gov
Phone: (505) 667-8161

Technology transfer contact
John B. Mott, jmott@lanl.gov
Phone: (505) 665-0883